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Original article

Antibacterial activity of colistin and tigecycline against Enterobacteriaceae and *Acinetobacter* clinical isolates in Sohag University Hospital

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ABSTRACT

Background: Enterobacteriaceae are very common in nosocomial and community-acquired illnesses. These organisms have developed a progressive resistance to a number of antibiotic classes, including carbapenems, which are frequently used as a last resort to treat infections caused by isolates that produce extended-spectrum β-lactamases (ESBLs) all over the world. The purpose of this investigation was to determine the in vitro susceptibility of strains of Acinetobacter and Enterobacteriaceae to tigecycline and colistin, as well as to identify the colistin resistance gene mcr-1 in each isolated strain. **Methodology:** Enterobacteriaceae and Acinetobacter strains from different clinical samples were isolated on suitable media and identified manually. Confirmation of manual identification of bacterial isolates, identification to species level and determination of antibiotic susceptibility was done using vitek-2 system. Evaluation of invitro susceptibility of Enterobacteriaceae and Acinetobacter strains to colistin by colistin elution test and tigecycline by disc diffusion test. Detection of colistin resistance gene mcr-1 in all isolated strains by conventional PCR and comparing colistin resistance phenotypically and genotypically. **Results:** Among the study strains 16 (14.3%) were resistant to colistin while 13 (11.6%) were resistant to tigecycline. The most common organism to be resistant to colistin was *Kl. Pneumoniae* (37.5%), followed by *E. coli* (31.3%). Higher resistance to tigecycline was observed among *E. coli* (46.2%) followed by *K. pneumoniae* (23.1%)**.** mcr-1 gene was detected in eight (7.14%) strains, from which 50 % are phenotypically resistant to colistin. **Conclusion:** there is increasing concern about the emergence of clinical MDR microorganisms resistant to colistin, an antibiotic of last resort, since it causes infectious illnesses that are thus challenging to treat.

Introduction

Antimicrobial resistance is currently one of the biggest issues facing health care systems throughout the world. As a result, the health infrastructure becomes unstable and expenses rise [1].

Antimicrobial resistance is linked to more than 35,000 fatalities annually, according to a recent report from the Centers for Disease Control and Prevention (CDC). A major contributing factor to the issue is the rise in carbapenem-resistant Gram-negative bacteria [2].

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Enterobacteriaceae are very common in nosocomial and community-acquired illnesses. These organisms have developed a progressive resistance to a number of antibiotic classes, including carbapenems, which are frequently used as a last resort to treat infections caused by isolates that produce extended-spectrum β-lactamases (ESBLs) all over the world [3].

Numerous intrahospital bloodstream, respiratory, urinary tract, and intraabdominal infections are caused by carbapenem-resistant Enterobacteriacea (CRE) isolates, which continue to pose a serious risk to public health [3]. Life-threatening infections, which pose a serious danger to global health and have fatality rates of 40–50%, could result from the establishment and dissemination of carbapenem-resistant Enterobacteriaceae (CRE) [4].

One of the most dangerous multidrug-resistant (MDR) nosocomial infections is Acinetobacter baumannii (A. baumannii). Pneumonia, bloodstream infections, urinary tract infections, and skin and wound infections are the main side effects linked to infections caused by different strains of MDR A. baumannii. Because there are few effective treatment options for these bacteria, the World Health Organization and the Centers for Disease Control and Prevention have recognized it as a critical priority pathogen, highlighting the urgent need for more research to address this challenge [3].

The usage of polymyxin, a last-resort medication for severe bacterial infections, has increased due to the prevalence of severely drug-resistant and multidrug-resistant (MDR) pathogens. Polymyxins are non-ribosomal, cyclic oligopeptides that have five main chemical components: polymyxins A, B, C, D, and E. these chemicals form a cyclic heptapeptide. These substances are distinguished by differences in their side chains of fatty acids and amino acid sequences. The prime representatives of polymyxin that have been used in clinical practice are polymyxin B and polymyxin E (colistin) [5].

Colistin works by reacting with the lipopolysaccharides on gram-negative bacteria's outer membrane, causing membrane damage that ultimately results in bacterial death. There are two ways that colistin resistance arises: plasmid resistance or chromosomal abnormalities. The PmrA/PmrB and PhoP/PhoQ expressing genes experience chromosomal alterations that result in changes to or even deletion of lipid molecules. The use of colistin is linked to these alterations. However, the presence of a plasmid-mediated mcr-1 gene that encodes the phosphoethanolamine transferase enzyme, which causes phosphoethanolamine to be transferred to lipid A, imparts colistin resistance even in the absence of prior exposure to colistin [6].

Tigecycline is an antibacterial drug of the tetracycline class that was created to treat polymicrobial MDR infections caused by both Gram-positive and Gram-negative bacteria. The Food and Drug Administration (FDA) approved tigecycline, sometimes referred to as GAR-936 or Tygacil, as the first and only glycylcycline class of semisynthetic medicines that can be given parenterally [7].

Patients and methods

This is a cross sectional study that was carried out in Medical Microbiology and Immunology Department, Sohag faculty of Medicine and Sohag University hospitals and extended along 1 year From August 2022 to August 2023. The study included 200 patients with different nosocomial infections recruited from different departments of Sohag University hospitals from which 112 were identified as *Enterobacteriaceae* and *Acinetobacter*. A written consent was obtained from each participant to be enrolled in the study. The local Ethical Committee of Faculty of Medicine, Sohag University, accepted the study protocol.

- **Sample processing:**

Various clinical samples were collected in an entirely aseptic setting. Urine, sputum, and endotracheal aspirate samples were collected in dry, sterile, tightly sealed plastic cups, while pus was collected using sterile cotton swabs. Simple blood culture bottles were utilized to collect blood samples, and they were cultured at 37° C with MacConkey media subcultures performed every other day. After centrifuging the samples for 10 minutes at 3000 rpm, Gram stain was applied to the deposit. Using a calibrated 10-microliter loop, the bacterial count was performed to diagnose urinary tract infections (UTIs) if there were 105 CFUs per milliliter or greater. Prior to inoculation on MacConkey medium (Oxoid, UK), all samples were fortified with nutrient broth for 24 hours at 37°C. Subcultures were conducted on eosin methylene blue media (Oxoid, UK).

- **Identification of the isolates at species level:**

Confirmation of manual identification of bacterial isolates and identification to species level was done using automated identification system **(Vitek- 2 BIOMÉRIEUX, France)**.

- **Antibiotic sensitivity testing:**

Susceptibility of isolated Enterobacteriaceae and Acinetobacter strains to different antibiotics was done by **(Vitek- 2 BIOMÉRIEUX, France)**.

- **Invitro susceptibility testing of isolated Enterobacteriaceae and Acinetobacter strains to tigecycline:**

Using disc diffusion (a modified Kirby-Bauer method), the susceptibility of isolated Enterobacteriaceae and Acinetobacter to tigecycline (15 µg) was examined [8, 9, 10], and [11].

Invitro susceptibility testing of isolated Enterobacteriaceae and Acinetobacter strains to colistin: (according to Colistin disc elution test) by using 10 µg colistin sulfate discs and Cation adjusted Mueller-Hinton broth (CAMHB) [12].

- **Detection of colistin resistance gene by simple qualitative PCR**

Simple qualitative polymerase chain reaction was performed for all isolated Enterobacteriaceae and Acinetobacter as the gold standard for identification of genes responsible for colistin resistance.

1) **DNA extraction by boiling method**
2) **DNA amplification**

Master mix: (COSMO PCR RED M.MIX, Willofort, UK, catalog number W10203001): The *COSMO* PCR RED Master Mix is a ready to use solution that can be used for amplification.

The primer sequences used in PCR assay for detection of mcr-1 gene in MDR Gram negative bacteria resistant to colistin are shown in table (1).

PCR protocol:

Amplification of the target gene by using a Biometra thermal cycler -T Gradient software version 5.0 PCR system according to [15, 16].

1) **Detection of the target gene by agarose gel electrophoresis:**

The PCR products were separated by electrophoresis in a 2 % agarose gel.

Statistical analysis:

The collected data were coded and verified prior to computerized data entry. The collected data were statistically analysed using Statistical Package for the Social Science (SPSS) version 26 program and expressed in tables. Microsoft 365 Excel was used to get graphs. The data were tested for normality by Kolmogorov-Smirnov. Chi-square exact was used for nominal data. Annova was used for parametric data. In all analyses, P value < 0.05 indicated statistical significance**.**

Results

Our study was carried out at Medical Microbiology and Immunology Department, Faculty of Medicine and Sohag University Hospitals in the period from August 2022 to August 2023. The study included 200 patients with different types of nosocomial infections from which 112 were identified as *Enterobacteriaceae* and *Acinetobacter*. The patient ages ranged from 2-93 years, the mean age ± SD was 40.1±25.2. Males represented 65.2% and females represented 45% of all cases.

The highest percentage of isolation was from urinary tract infections (25.9%), while the lowest percentage was from VAP (12.5%) (Figure 2). 26.8% of isolates were from urine samples, 23.2% from wound swabs, 23.2% from sputum, 15.2 % from blood cultures and 11.6 % were from endotracheal aspirates (figure 3).

Twenty-two (19.6%) strains were isolated from patients in internal medicine department while 21 (18.8%) strains were isolated from patients in general surgery department and 18 (16.1%) strains were isolated from patients in ICU (table 4).

In vitro antibiotic susceptibility testing of the isolated strains by Vitek 2 system:

Antibiotic resistance was highly prevalent in *Kl. Pneumoniae* to the following antibiotics; ampicillin sulbactam (39.6%), piperacillin tazobactam (39.6%), Ampicillin resistance (37.5%), Cefoxitin resistance (38 %), Ceftazidime (37.1%), ceftriaxone (38.5%) and Tobramycin resistance was (37.6 %)

While antibiotic resistance was highly prevalent in *E.coli* to the following antibiotics: gentamycin resistance (35.6%), Levofloxacin resistance (36%) and Trimethoprim/sulphamexazole resistance (37.4%).

According to the tested panel of antibiotics in Vitek2 system panel, most of the study strains were extreme drug resistant (XDR) (49.1%) and

28.6% were possible pan drug resistant while 9.8% were multidrug resistant (Tab 5).

Sixteen percent of isolated *klebseilla pneumoniae* were MDR, 80%of isolated *proteus mirabilis* strains were XDR 50% of isolated *citobacter baumani* were possible PDR (Table 6).

Among the studied strains 16 (14.3%) were resistant to colistin while 13 (11.6%) were resistant to tigecycline and 15 (13.4%) were ESBL (Table 7).

There was no significant correlation between ESBL production and tigecycline resistance (Table 9).

The most common organism to be resistant to colistin was *Kl. Pneumoniae* (6 strains -37.5%), followed by *E.coli* (5 strains – 31.3%) while to tigecycline was *E.coli* (6 strains -46.2%), followed by *Kl. Pneumoniae* (3strains – 23.1%) (Table 10).

Detection of colistin resistance gene (mcr-1) by simple qualitative PCR

Colistin resistance gene (mcr-1) was detected in eight strains (7.14%) out of all isolated strains (112) (Figure 4).

There is highly significant relation between phenotypic resistance of colistin (detected by disc elution test) and genotypic resistance (mcr-1) gene, with P value <0.001 (Table 11).

mcr -1 gene was detected in three strains of *klebseilla pneumoniae* and three strains of *klebseilla aerogenes* and in two strains of *E.coli* (Table 12).

mcr-1 gene was detected in six strains that were negative ESBL and in two strains that were positive ESBL so there is insignificant correlation between mcr-1 gene and ESBL production (Table 13).

Sixty two percent of isolated positive mcr-1 gene were XDR while 25.5% were PDR (Tab 14).

Fifty percent of strains positive mcr-1 gene were isolated from blood samples in patients with PUO while 37.5 %were isolated from sputum (Table 15)

Table 1. The primer sequences used in PCR assays for detection of *mcr-1* gene [13, 14].

Gene	Primer	Nucleotide Sequence	Amplicon size
mcr-1	**Forward** **Reverse**	5′ AGTCCGTTTGTTCTTGTGGC 3′ 5′ AGATCCTTGGTCTCGGCTTG 3′	320 bp

Table 2. Colistin and tigecycline resistance and ESBL distribution among the isolated strains.

Colistin	**Frequency**	**Percent**
R	**16**	**14.3%**
S	**96**	**85.7%**
Tigecycline	**Frequency**	**Percent**
R	**13**	**11.6%**
S	**99**	**88.4%**
ESBL	**Frequency**	**Percent**
Positive	**15**	**13.4%**
Negative	**97**	**86.6%**

Table 3. Colistin resistance related to ESBL in the study.

			Colistin		**Total**	**P value**
			Resistance	**Susceptible**		
ESBL	**Negative**	Number	13	84	97	0.5
		%	81.3%	87.5%	86.6%	
	Positive	Number	3	12	15	
		%	18.8%	12.5%	13.4%	
Total		Number	16	96	112	
		%	100.0%	100.0%	100.0%	

There was no significant correlation between ESBL production and colistin resistance (Table 8).

Table 4. Tigecycline resistance related to ESBL in the study.

			Tigecycline			P value
			Resistance	Susceptible	Total	
ESBL	Negative	Number	11	86	97	0.8
		%	84.6%	86.9%	86.6%	
	Positive	Number	2	13	15	
		%	15.4%	13.1%	13.4%	
Total		Number	13	99	112	
		%	100.0%	100.0%	100.0%	

Table 5. Distribution of tigecycline and colistin resistance among the isolated strains.

Microorganism		Colistin		Tigecycline		Total
		Resistance	Susceptible	Resistance	Susceptible	
Kl. Pneumoniae	Number	6	36	3	39	42
	%	37.5%	37.5%	23.1%	39.4%	37.5%
E. coli	Number	5	31	6	30	36
	%	31.3%	32.3%	46.2%	30.3%	32.1%
Kl. aerogens	Number	3	11	2	12	14
	%	18.8%	11.5%	15.4%	12.1%	12.5%
	%	6.3%	3.1%	0.0%	4.0%	3.6%
Kl. Oxytoca	Number	0	6	2	4	6
	%	0.0%	6.3%	15.4%	4.0%	5.4%
Proteus mirabilis	Number	1	4	0	5	5
	%	6.3%	4.2%	0.0%	5.1%	4.5%
Total	Number	16	96	13	99	112
	%	100.0%	100.0%	100%	100.0%	100.0%
P value		0.8		0.4		

Table 6. Comparison of colistin resistance phenotypically and genotypically.

			mcr-1 gene		Total	P value By chi-square
			Negative	Positive		
Colistin elution test	Positive	Number	8	8	16	<0.001
		%	7.1%	7.1%	14.3%	
	Negative	Number	96	0	96	
		%	85.7%	0.0%	85.7%	

Table 7. Frequency of mcr1 gene among the isolated strains

Type of department		mcr-1gene		Total	P value by chi-square
		Negative	Positive		
Kl. Pneumoniae	N	39	3	42	0.4
	%	92.9%	7.1%	100%	
E. coli	N	34	2	36	
	%	94.4%	5.6 %	100 %	
Kl. Aerogens	N	11	3	14	
	%	78.5%	21.5%	100%	
Kl. Oxytoca	N	6	0	6	
	%	100%	0.0%	100%	
Proteus mirabilis	N	5	0	5	
	%	100%	0.0%	100%	
Acinetobacter bumanii	N	5	0	5	
	%	100%	0.0%	100%	
***Citrobacter* spp.**	N	4	0	4	
	%	100%	0.0%	100%	
Total	N (%)	104 (100%)	8 (100%)	112 (100%)	

Table 8. Frequency of mcr-1 gene among ESBL strains.

ESBL		mcr1gene Negative	mcr1gene Positive	Total	P value by chi-square
Negative	N	91	6	97	0.3
	%	87.5%	75.0%	86.6%	
Positive	N	13	2	15	
	%	12.5%	25.0%	13.4%	
Total	N	104	8	112	
	%	100%	100.0%	100.0%	

Table 9. Frequency of mcr1 gene according to drug resistance.

Drug resistance		mcr1gene Negative	mcr1gene Positive	Total	P value by chi-square
MDR	N	11	0	11	0.7
	%	10.6%	0.0%	9.8%	
XDR	N	50	5	55	
	%	48.1%	62.5%	49.1%	
PDR	N	30	2	32	
	%	28.8%	25.0%	28.6%	
Sensitive	N	13	1	14	
	%	12.5%	12.5%	12.5%	
Total	N	104	8	112	
	%	100%	100.0%	100.0%	

Table 10. Distribution of mcr1 gene according to type of infection.

Infection		mcr1gene Negative	mcr1gene Positive	Total	P value
Chest infection	**N**	23	3	26	0.02
	%	22.1%	37.5%	23.2%	
VAP	**N**	14	0	14	
	%	13.5%	0.0%	12.5%	
PUO	**N**	13	4	17	
	%	12.5%	50.0%	15.2%	
UTI	**N**	29	0	29	
	%	27.9%	0.0%	25.9%	
wound infection	**N**	25	1	26	
	%	24.0%	12.5%	23.2%	
Total	**N**	104	8	112	
	%	100.0%	100.0%	100.0%	

Figure 1. Colistin elution test, A and B are susceptible strains while, C and D are resistant strains.

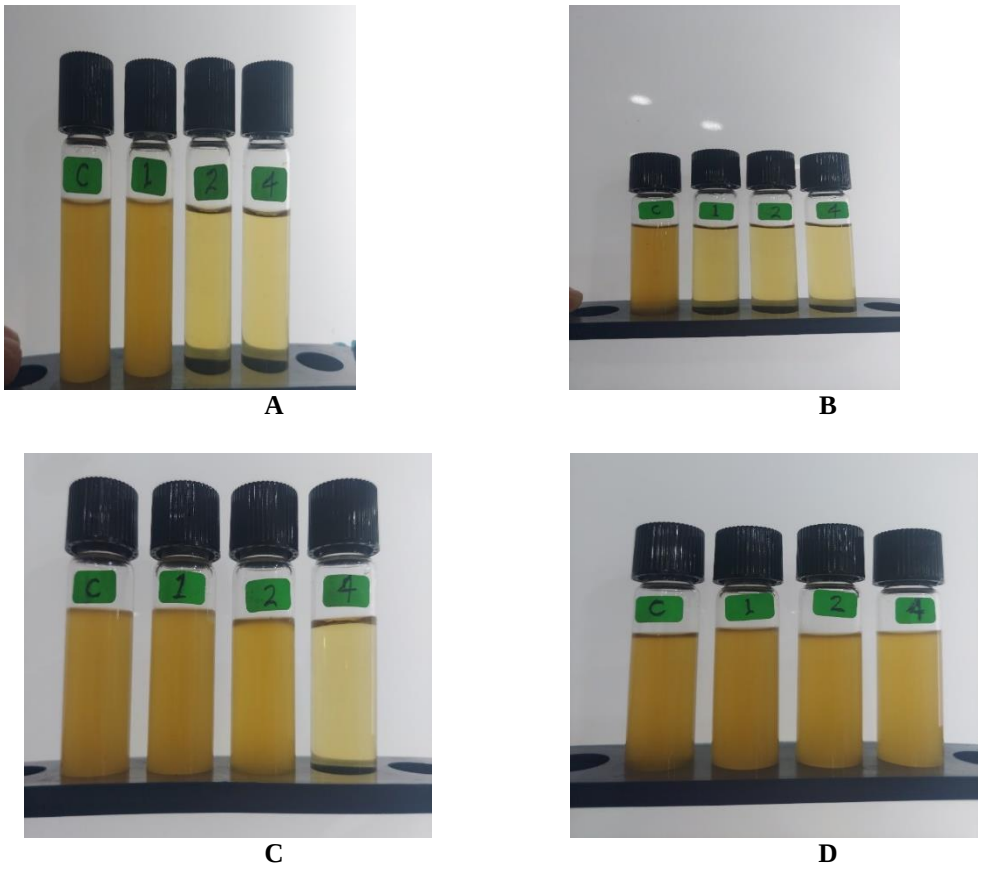


Figure 2. Type of infection in the participants.

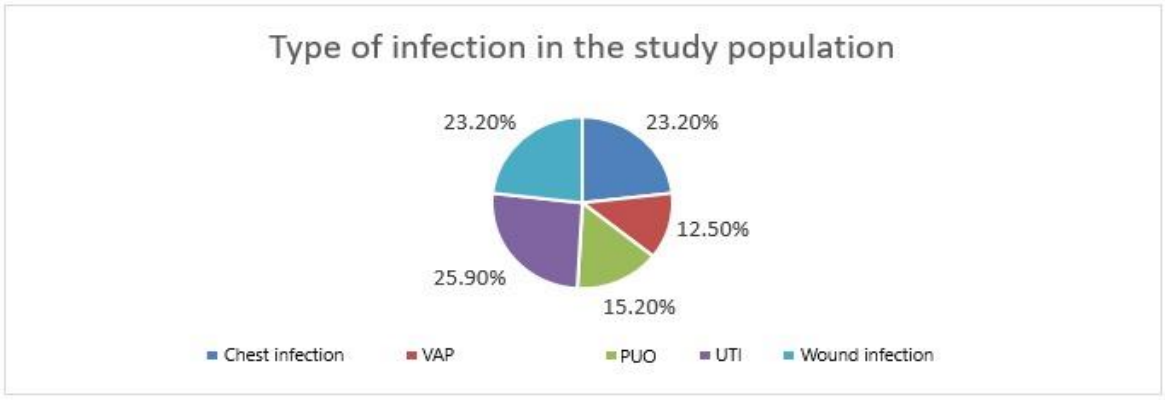


Figure 3. Type of samples from the studied patients.

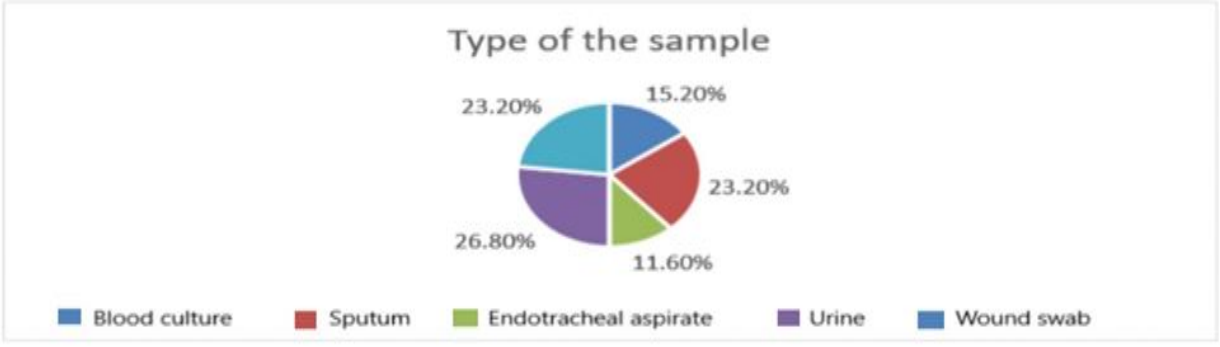


Figure 4. mcr-1 gene Agarose gel electrophoresis (2%) of PCR product of amplified mcr-1 gene (320bp). Lane M: DNA ladder (100bp); Lane 2 & 5: positive amplicon; Lane 1, 3, 4, 6, 7: negative amplicon

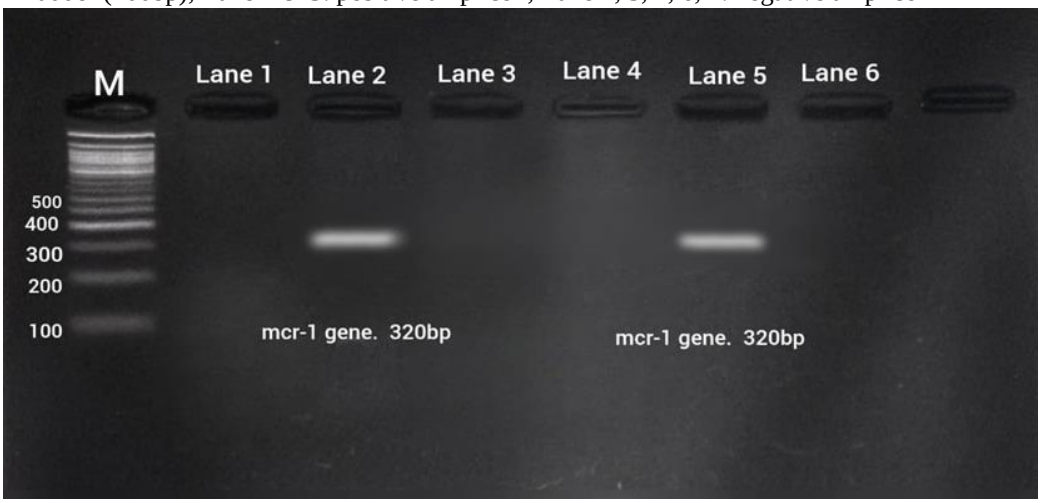
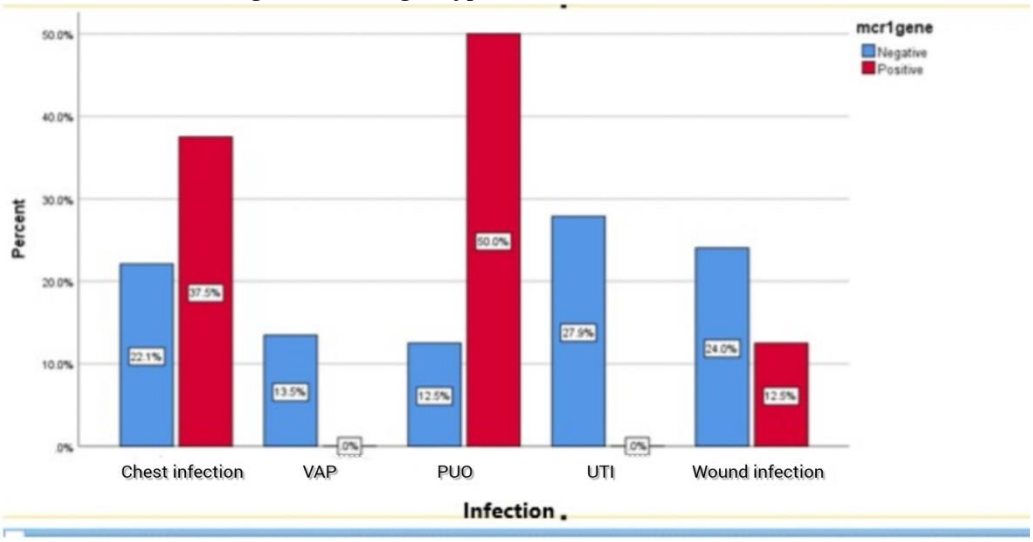


Figure 4. Distribution of mcr1 gene according to type of infection.



Discussion

There are very limited antimicrobial choices available due to growing resistance to most other antibiotic classes, which made choosing an adequate antibiotic regimen to treat infections with CRE extremely difficult. These choices include ceftazidime-avibactam, tigecycline, polymyxins, and more recent aminoglycosides.

Effective techniques for early detection and control should be implemented to prevent the possible ongoing proliferation of these carbapenem-resistant bacteria, since the growing resistance of CPE to current antibiotics such as tigecycline and colistin poses a threat to clinical therapy. To comprehend the mechanism of drug resistance, the carbapenemases can be distinguished using a combination of the disc test and MHT. With consistent monitoring to follow the emergence and spread of resistance, tigecycline may be useful. For CRE infections, colistin is still a good choice.

Tigecycline is a recently developed antibiotic that is primarily used to treat infections brought on by organisms that are resistant to many drugs. The most common pathogens that tigecycline is effective against include Klebsiella species, E. coli, Acinetobacter species, and Enterobacter species. Excellent in vitro action against bacteria that produce ESBL has been demonstrated by tigecycline. Regular monitoring of tigecycline use is necessary to track the emergence of resistance. When used in conjunction with other antibiotics to treat life-threatening illnesses and infections

brought on by MDR bacteria, it should be used as a backup antibiotic.

According to the present study the mean age of the studied patients ± SD was 40.1±25.2 years, this is the same as **Emara, Manar MM.,2019** [17]. The gender distribution among the studied patients was **73** males **(65.2%)** and **39** females **(45%)** i.e. about, this result was similar to **Emara, Manar MM.,2019** (17). and **Remash *et al.*, 2024** [18].

Most of enterobacteriacea strains in the study were isolated from urine samples; this is similar to that reported by **Abavisani *et al.*, 2023** [19].

According to our study results, the most common organism to be resistant to colistin was *Kl. Pneumoniae* (6 strains -37.5%) ,followed by *E.coli* (5 strains – 31.3%) while resistance to tigecycline was mostly prevalent in *E.coli* (6 strains -46.2%) ,followed by *Kl. Pneumoniae* (3strains – 23.1%) this is vice versa to **Remash *et al*.,2024** [18]. In addition, there were no relation between ESBL production and resistance to tigecycline, this disagreed with **Remash *et al.*, 2024** [18].who said that tigecycline resistance is more common among ESBL producer enterobacteriacea. And the most common antibiotic resistance mechanism evolving among the family Enterobacterales is through the development of ESBL production **Remash *et al.*,2024** [18], this is disagreed with our study results that said that ESBL producers represented only (13.4%) of the study strains.

Among the study strains 16 (14.3%) were phenotypically resistant to colistin, this results is similar to results of **Sundaresan and Rathinavelan 2023** [20] and **Sindelar, 2024** [21]. However, this result is less than that of **Abavisani *et al.*, 2023** [19] who said (41%) of their study strains were resistant to colistin but more than that of **Bhavyasri *et al.*,2020** [22], this could be explained by either the presence of chromosomal-mediated resistance, or the presence of other *mcr* gene variants. About 13 *mcr-1* subgroups were already described in several countries, differing from *mcr-1* by only one nucleotide. In addition, other nine-mcr variants have been described

The most common organism to be resistant to colistin was *Kl. Pneumoniae (*6 strains-37.5%), this result is totally agreed with **Sundaresan and Rathinavelan 2023** [20] and **Sindelar, 2024** [21] but vice versa to **Abavisani *et al.*, 2023** [19].

According the study result tigecycline susceptibility in enterobacteriacea was high (88.4%), this is agreed with **Pusz-Bochenska *et al.*, 2022 (23).** Higher resistance to tigecycline was observed among *E. coli* (46.2%) followed by *K. pneumoniae* (23.1%) in our study strains; this is vice versa to **Sundaresan and Rathinavelan 2023** [20].

XDR was defined as non-susceptibility to at least one agent in all but two or fewer antimicrobial categories (i.e., bacterial isolates remain susceptible to only one or two categories), PDR as non-susceptibility to all agents in all antimicrobial categories, and MDR as non-susceptibility to at least one agent in three or more antimicrobial categories [24].

Infections with MDR, PDR, and XDR bugs were mostly observed in intensive care unit patients. Patients who require central lines, long catheterizations, and extended hospital stays are always at risk of getting resistant diseases. Patients and healthcare providers still face clinical and financial challenges because of MDRs. The issue is that bacteria are developing resistance much more quickly than the recently released medication **Ghogale et al., 2024** [24]

According to the tested panel of antibiotics in Vitek2 system panel , Most of the study strains were extreme drug resistant (XDR) (49.1%) and 28.6% were pan drug resistant while 9.8% were multidrug resistant**,** these results were similar to **Ghogale *et al.*, 2024** [25].

Sixteen percent of isolated klebseilla pneumoniae were MDR, 80%of isolated proteus mirabilis strains were XDR 50% of isolated citobacter baumani were PDR, This a high level of resistance against tested antimicrobials; as These findings also agrees with **Samantha *et al.*, 2020** [25], who reported marked resistance to the third generation cephalosporin (60%), fourth generation cephalosporin (78%), and carbapenem antibiotics (50%). Another study found resistance to ciprofloxacin, piperacillin/tazobactam and nitrofurantoin was 90% for each one, 30% to carbapenems, and 20% to aminoglycosides. This variability in resistance pattern can be explained by difference in antibiotics policy applied in health care settings within different geographical regions.

mcr-1 gene was detected in (7.14%) of the study strains, this is similar to **Ali *et al.*,2022** [26] while it was higher than **Makled, *et al.* , 2023** [27],the gene was detected in 50% of the strains that are phenotypically resistant to colistin Therefore, it

is concluded that the colistin resistance observed in 50% of *Enterobacteriaceae* isolates in our region is not due to the mcr genes screened, but to different resistance development mechanisms. while in the study of **Ghasemi *et al*.,2023**, [28] the gene was not detected.

Ongoing transfer of *mcr-1* may lead to higher rates of poor treatment outcomes and consequently greater morbidity and mortality rates. Thus, surveillance for colistin resistance mediated by this gene should be conducted and studies should involve greater collection of isolates.

There is significant relation between phenotypically resistance of colistin (detected by disc elusion test) and genotypic resistance (mce-1) gene, with P value <0.001, this agreed with **Gonzales Escalante *et al*., 2020** [29].

mcr -1 gene was detected in 3 strains of klebseilla pneumoniae and 3 strains of klebseilla aerogenes and in 2 strains of E.coli ,these results were vice versa to **Yaghoubi *et al*.,2022** [30]

The emergence of multidrug-resistant (MDR) Enterobacterales isolated from humans and animals has become a great concern worldwide, and resistance to colistin in coexistence with β-lactams resistant genes compromises the effectiveness of antimicrobial drugs **Murray *et al*., 2022** [31]

mcr-1 gene was detected in 6 strains that were negative ESBL and in 2 strains that were positive ESBL so there is insignificant correlation between mcr-1 gene and ESBL, this is vice versa to **Murray *et al*., 2022** [32] , who found strong relation between both items.

The co-existence of the colistin resistance (*mcr*) gene with multiple drug-resistance genes has raised concerns about the possibility of the development of pan-drug-resistant bacteria that will complicate treatment. According to the present study there were 62.5% of isolated positive mcr-1 gene were XDR while 25.5% were PDR, these results were similar to **Karim *et al*., 2023** [32].

Fifty percent of mcr-1 positive strains were from patients admitted in ICU, these results near that of **Mirzaei *et al*., 2023** [33].

Conclusion

The most common organism to be resistant to colistin was *Kl. Pneumoniae* (37.5%), followed by *E.coli* (31.3%) while resistance to tigecycline was mostly prevalent in *E.coli* (46.2%), followed by *Kl. Pneumoniae* (23.1%), According to the tested panel of antibiotics in Vitek2 system, most of the studied strains were extreme drug resistant (49.1%) and 28.6% were pan drug resistant while 9.8% were multidrug resistant**.** Sixteen percent of isolated *klebseilla pneumoniae* were MDR , 80% of isolated *proteus mirabilis* strains were XDR and 50% of isolated *acenitobacter baumani* were PDR, mcr-1 gene was detected in 8 strains (7.14%) of the studied strains (112). mcr -1 gene was detected in 3 strains *of klebseilla pneumoniae* and 3 strains of *klebseilla aerogenes* and in 2 strains of *E.coli*.

Conflict of interest

None declared.

Financial disclosure

None declared. No financial disclosure

Data availability

All data are available from the corresponding author upon reasonable request.

Authors' contribution

All authors made significant contributions to the work presented, including study design, data collection, analysis, and interpretation. They also contributed to the article's writing, revising, or critical evaluation, gave final approval for the version to be published.

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